Electronic Supplementary Material (ESI) for Soft Matter.

NIR light, pH, and redox-triple responsive nanogels for controlled release

Supporting Information

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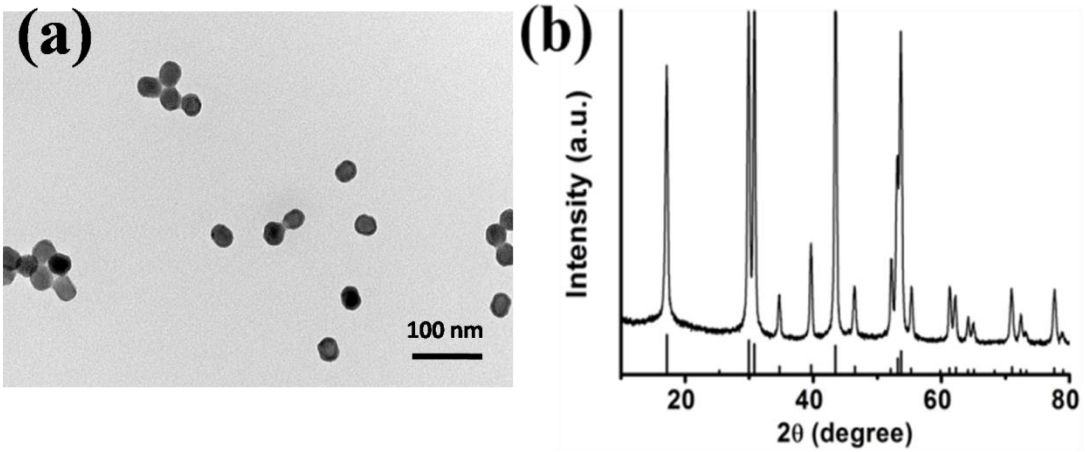


Fig. S1(a)Transmission electron microscopy (TEM) image of the UCNP; (b)XRD patterns of β-$NaYbF_4$: 25% Yb, 0.5% Tm.

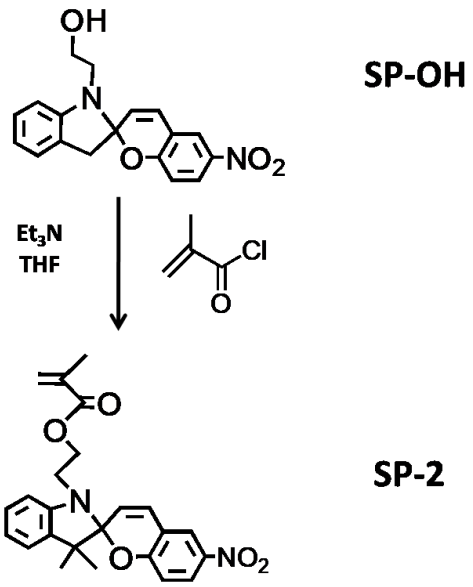


Fig. S2 Synthetic route of SP-2.

SP-2 was prepared according to reported procedure [s1] and the synthetic route has been shown in Figure S2. ^{1}H NMR (300MHz, $CDCl_3$): 1.176(s,

6H,-C(CH_3)$_2$), 1.897 (s, 3H, =C-CH_3), 3.393–3.552 (m, 2H,-N-CH_2-), 4.273 (t, 2H, -O-CH_2-), 5.545 and 6.053 (s, 2H, =CH_2), 6.642–6.748 (d, 2H, Ar-Hand –CH=), 6.878–6.963 (m, 2H, Ar-H),7.073–7.104 (m, 1H,Ar-H), 7.172–7.240 (m,1H,Ar-H), 7.990–8.016 (m, 2H, Ar-H).

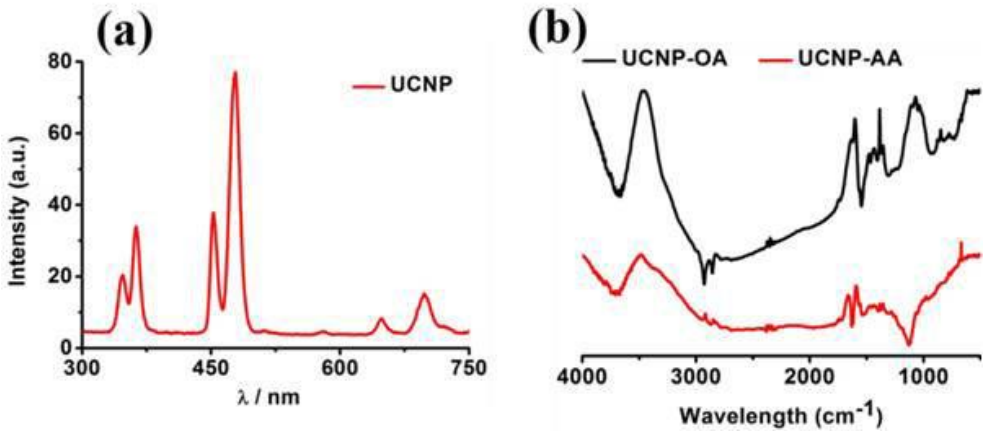


Fig. S3 (a) Upconversion luminescence spectrum of the synthesized UCNP-AA, excited at 980 nm; (b) Fourier transform infrared (FT-IR) spectra of the UCNP-OA (black) and UCNP-AA (red).

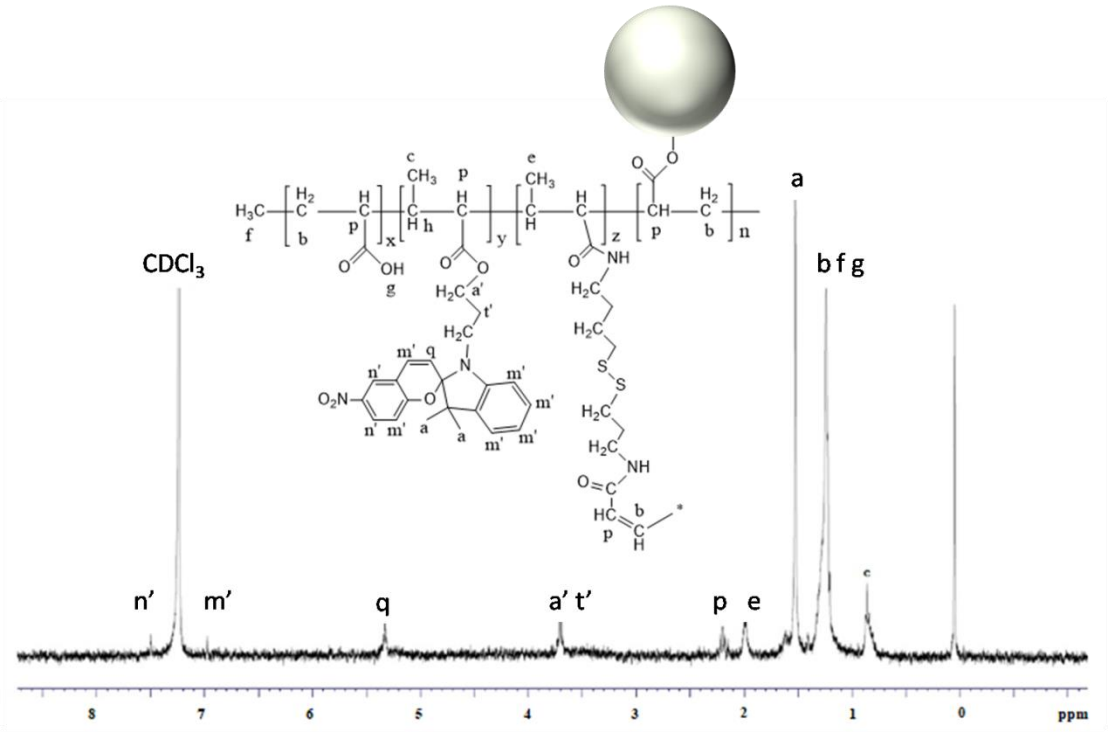


Fig.S4 ^{1}H NMR spectrum of UCNP-NGs in $CDCl_3$(300 MHz)

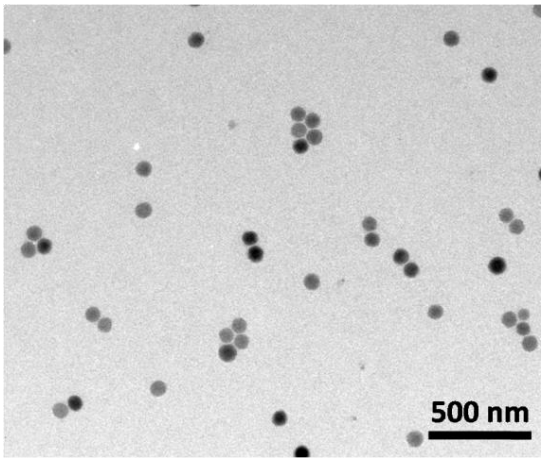


Fig. S5 TEM image of polymerized UCNP-AA.

The UCNP-AA was polymerized independent, which adopted the reaction conditions in the paper. Figure S5 showed that nanoparticles were dispersed, which indicated that UCNP-AA could not self-aggregate under the conditions of literature.

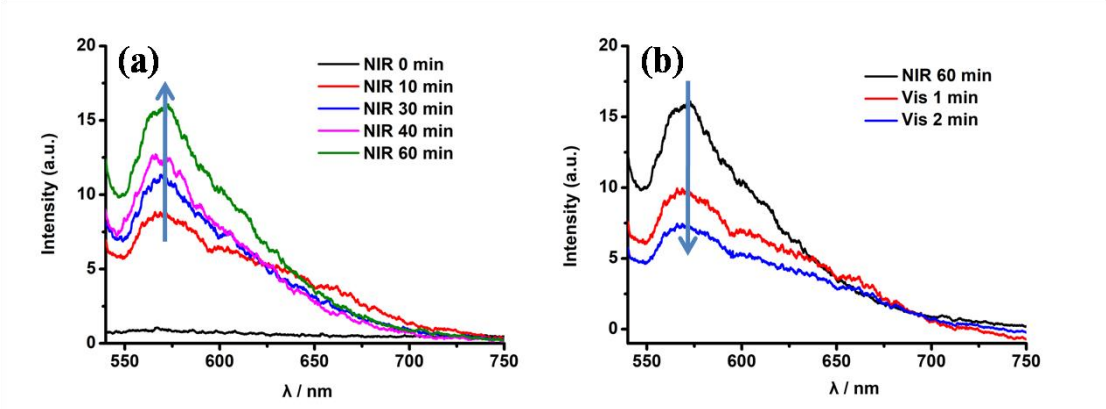


Fig.S6 The fluorescence spectra of the UCNP-NGs: (a) Irradiated with NIR light (980 nm, 4.3W cm^{-2}), (b) then irradiated with visible light (520 nm, 20 mW cm^{-2})

The MC structure is a fluorescent group, and the excitation wavelength of MC group is 565 nm. As shown in the Figure S6(a), the fluorescence intensity of MC increases with the increase of NIR irradiation time, which indicates that SP in the nanogel is transforming into MC after NIR

irradiation for a certain time. As shown in the Figure S6(b), the fluorescence intensity of MC decreases with the increase of visible irradiation time, which indicates that MC in the nanogel is transforming into SP after visible irradiation for a certain time.

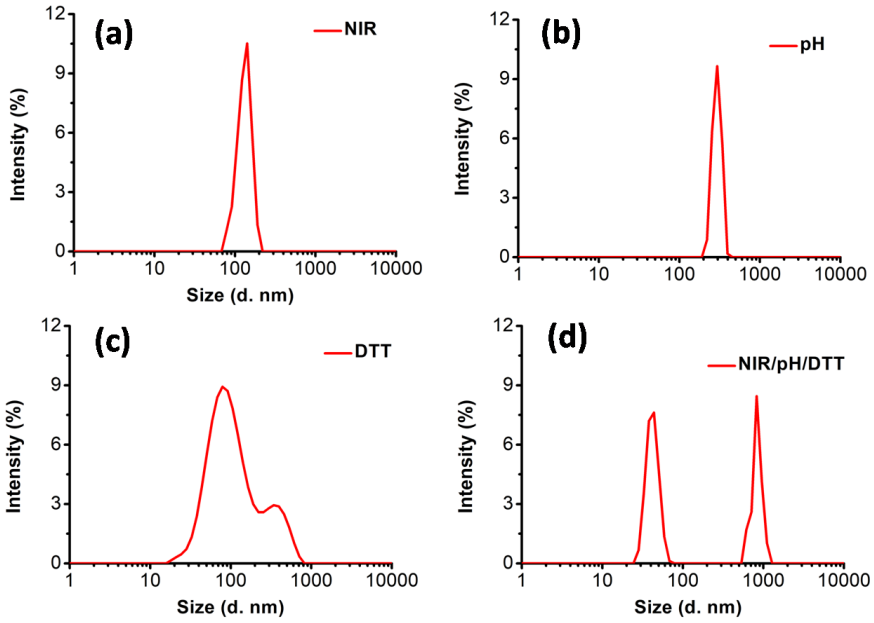


Fig. S7 Size distribution from DLS analysis of the UCNP-NGs under different stimuli: (a) without stimulation;(b) under NIR irradiation for 10 min; (c) at pH 5 for 12 h; (d) in the presence of DTT (4 mM) for 12 h; (e) combined stimulation of NIR light irradiation (3 min), pH 6 and in the presence of DTT (4 mM) for 12 h.

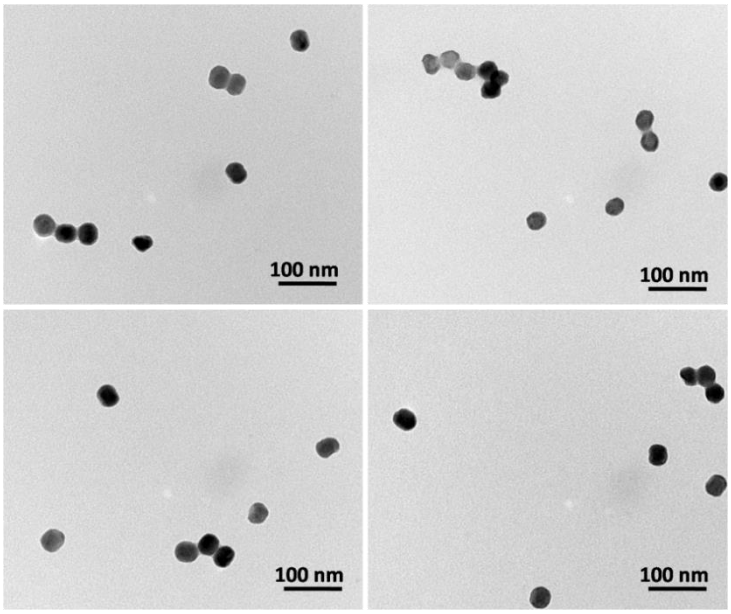


Fig.S8 The TEM images of UCNP-AA under different stimuli: (a) under NIR irradiation for 10 min; (b) at pH 5 for 12 h; (c) in the presence of DTT (4 mM) for 12 h ;(d) combined stimulation of NIR light irradiation (3 min), pH 6 and in the presence of DTT (4 mM) for 12 h.

As shown in Figure S8, under different stimuli, the morphology of UCNP-AA is basically consistent, indicating that the morphology changes of UNCP-NGs are mainly caused by stimulus-responsive polymers under different stimuli.

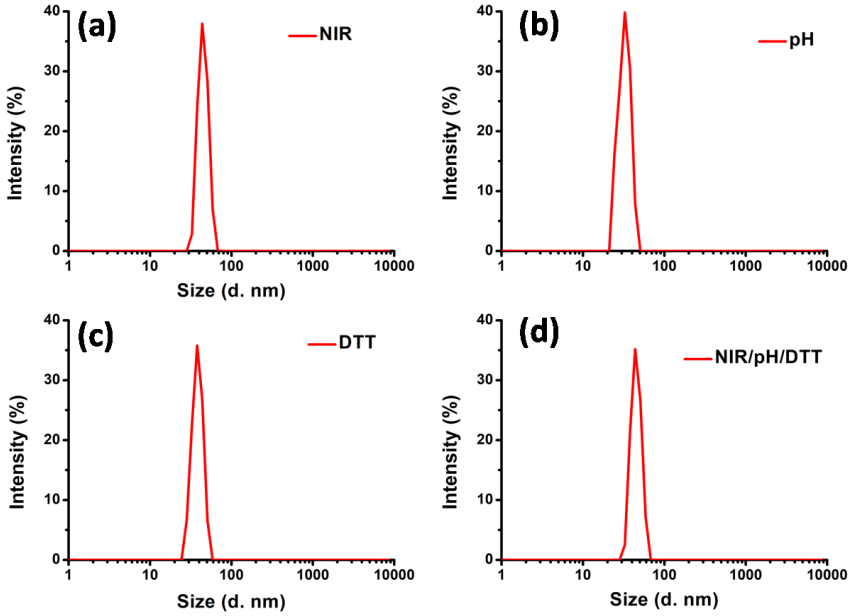


Fig.S9 Size distribution from DLS analysis of the UCNP-AA under different stimuli: (a)under NIR irradiation for 10 min;(b) at pH 5 for 12h; (c) in the presence of DTT (4 mM) for 12 h; (d)combined stimulation of NIR light irradiation (3 min), pH 6 and in the presence of DTT (4 mM) for 12 h.

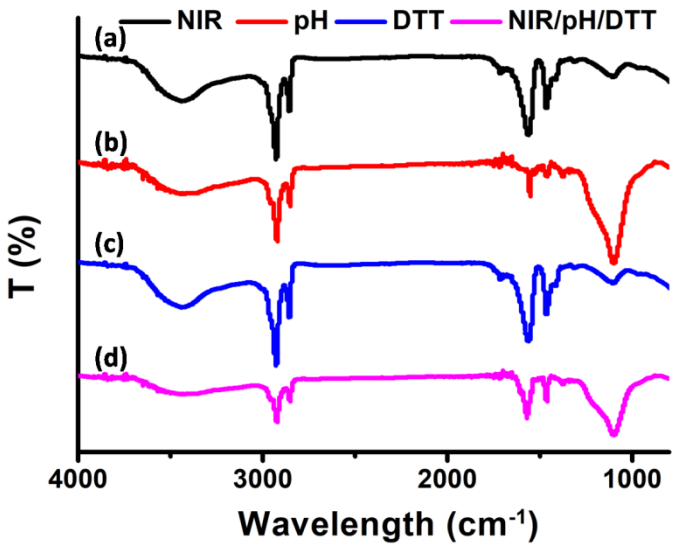


Fig.S10 FT-IR spectra of the UCNP-AA under different stimuli: (a)under NIR irradiation for 10 min;(b) at pH 5 for 12h; (c) in the

presence of DTT (4 mM) for 12 h; (d)combined stimulation of NIR light irradiation (3 min), pH 6 and in the presence of DTT (4 mM) for 12 h.

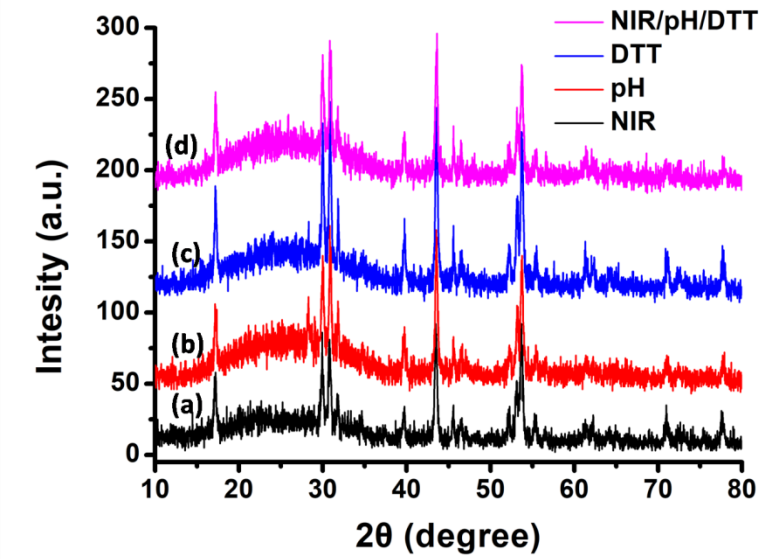


Fig.S11 XRD patterns of UCNP-AA under different stimuli: (a)under NIR irradiation for 10 min;(b) at pH 5 for 12h; (c) in the presence of DTT (4 mM) for 12 h; (d)combined stimulation of NIR light irradiation (3 min), pH 6 and in the presence of DTT (4 mM) for 12 h.

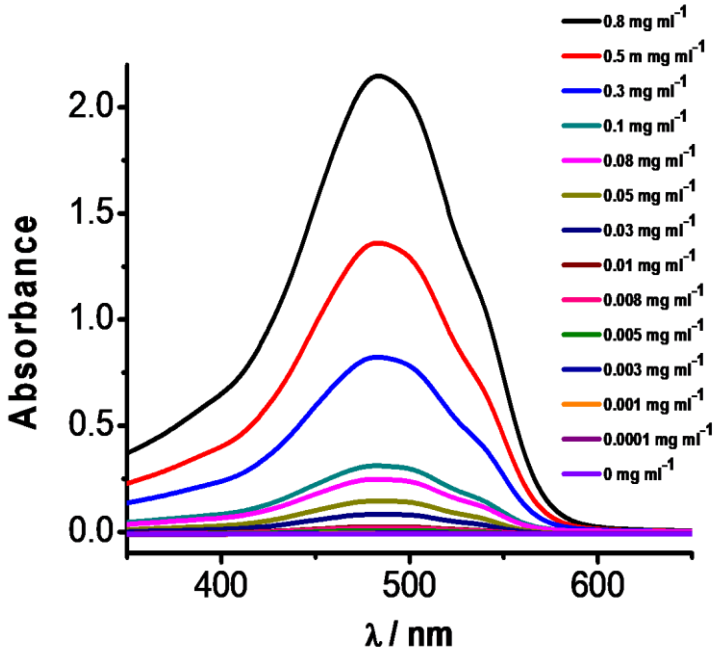


Fig. S12 UV-vis spectra of DOX with different concentrations.

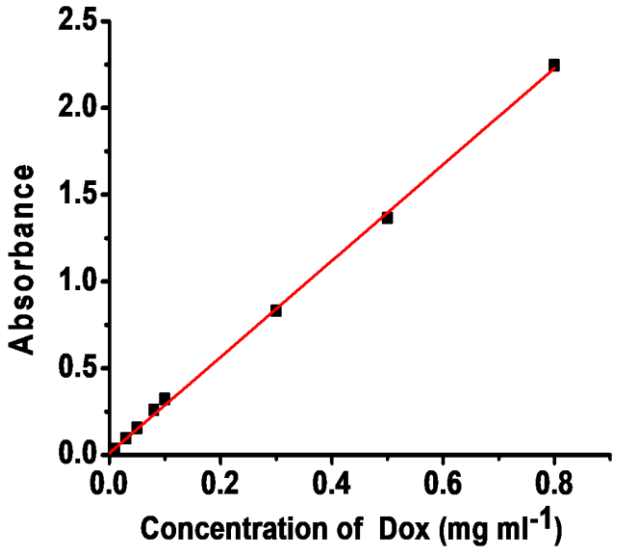


Fig. S13 DOX calibration curve.

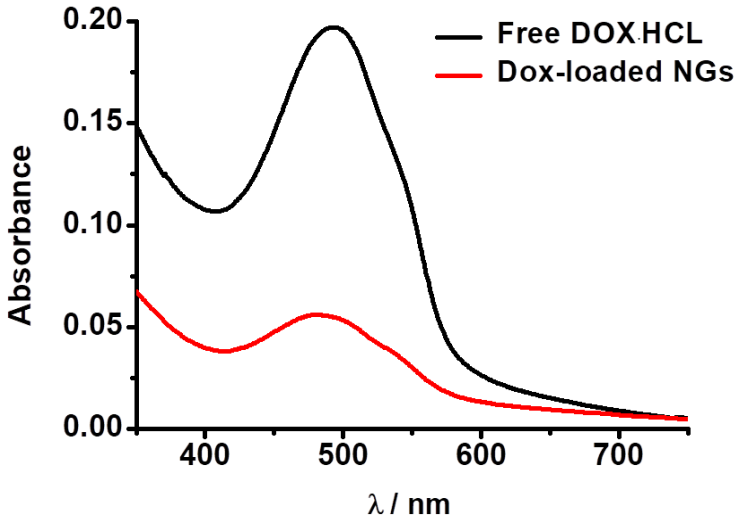


Fig.S14 UV-vis spectra of the UCNP-NGs mixed with DOX after 72 h dialysis (DOX initial concentration: 1 mg, red) and free DOX (1 mg, black).

DOX·HCl (1 mg) was dissolved in water (5 mL) and then UCNP-NGs (2 mg) were added to the solution, stirred at room temperature for 24 h. Then the mixture was subjected to dialysis (MWCO: 3500 Da) against distilled water for 72 hours to remove the free drug. The samples were lyophilized to obtain the DOX-loaded UCNP-NGs, which were kept at 4 ^{o}C for further study. All the drug loading processes were performed under dark. The DOX concentration was determined by spectrophotometry (λmax = 490 nm) using a DOX calibration curve (Figure S12). The loading capacity (LC) of UCNP-NGs was about 13% which was calculated by the following formula:

$$LC(wt\%) = \frac{weight\ of\ loaded\ Dox}{weight\ of\ NGs} \times 100\%$$

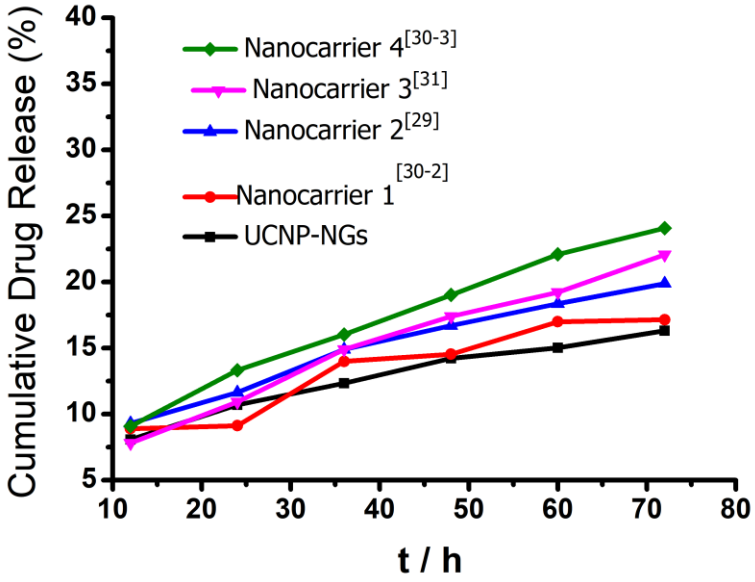
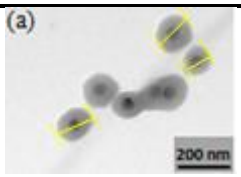
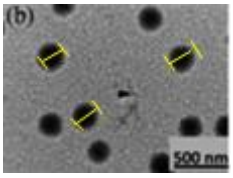
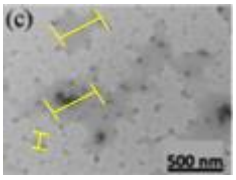
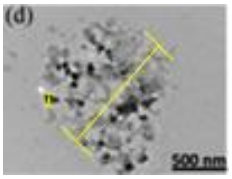


Fig.S15 The drug loaded stability of different nanoconpsites: (a) self-assembled nanohybrids; (b) self-assembled nano-micelles; (c) UCNP-NGs.

Table 1 Drug loading capacity of different Nanocarriers

Nanocarriers	Loading capacity
UCNP-NGs	13%
UCNPs@Polymer nanocomposites[31]	11%
NGs[28-1]	18%
PDMAEMA micelles[28-2]	19%

Table 2 Size distribution and change reason of UCNP-NGs under different stimuli

Stimuli	TEM image	From TEM	From DLS	Reason
NIR light		100-120 nm	98 nm	SP→MC
pH		220-280 nm	266 nm	SP→MCH^+
DTT		100-430 nm	105 nm 397 nm	S-S bonds broken
Combined stimulation		70-990 nm	91 nm 822 nm	SP→MC/ SP→MCH^+/ S-S bonds broken

References

[S1]S. Chen, F. Jiang, Z. Cao,G. Wang, Z. Dang, *Chem. Commun.*, 2015, **51**, 12633-12636.